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Real-World Effectiveness and Safety of Lurbinectedin for Small Cell Lung Cancer: Updates From Jazz EMERGE 402

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Background

- Lurbinectedin, a selective inhibitor of oncogenic transcription, received accelerated approval from the US Food and Drug Administration in June 2020—and is now available in a total of 18 territories around the world—as a monotherapy for the treatment of adults with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy[1-3]
- Approvals were based on results from a single-arm, open-label, phase 2 basket trial of 105 patients with relapsed SCLC (NCT02454972)[2-4]
  - Lurbinectedin had an overall response rate (ORR) of 35.2%, a median duration of response of 5.3 months, a median progression-free survival (PFS) of 3.5 months, a median overall survival (OS) of 9.3 months, and an acceptable and manageable safety profile[4]
  - Among enrolled patients, 35% were ≥65 years old, 43% were platinum-refractory (chemotherapy-free interval [CTFI] <90 days), and 93% received lurbinectedin in the second-line (2L) setting; per protocol, patients with active central nervous system (CNS) metastases were ineligible[4]
- Jazz EMERGE 402 (NCT04894591) is a prospective, single-arm, multicentre, phase 4 observational trial designed to assess the effectiveness and safety of lurbinectedin in a broad population of patients with extensive stage (ES)-SCLC in real-world clinical practice
  - An interim analysis from 171 patients was previously presented[5]

Objective

- Here, we report updated effectiveness and safety results in 265 patients treated with lurbinectedin from the Jazz EMERGE 402 trial

Methods

- Jazz EMERGE 402 included adult patients with ES-SCLC who were treated with lurbinectedin according to the local label in the US and Canada
- Patients were assessed by a physician and prescribed lurbinectedin per routine treatment practice prior to study enrolment; the use of granulocyte colony-stimulating factor (G-CSF) prophylaxis was documented
- Data were collected at baseline and during patient care from enrolment until death, withdrawal of consent, loss to follow-up, or 24 months elapsed (whichever occurred first)

Table 1. Endpoints for Jazz EMERGE 402

Primary Endpoints
• Investigator-assessed overall response rate per RECIST v1.1
Secondary Endpoints
• Progression-free survival
• Duration of response
• Disease control rate
• Overall survival
• Incidence and severity of adverse events
• Reasons for treatment discontinuation or dose reduction/delay

RECIST v1.1, Response Evaluation Criteria in Solid Tumours version 1.1.

- Effectiveness outcomes were assessed in all patients and in subgroups of interest, including by line of therapy (2L or third-line [3L]), CTFI (<90 days or ≥90 days), age (<65 years or ≥65 years), and the presence of CNS metastasis (yes or no)
- Safety and tolerability were assessed in all patients
- Outcomes for patients who received lurbinectedin as fourth-line or later therapy or in combination with other anticancer therapies are not reported separately here due to the small number of patients

Results

Table 2. Baseline Patient Demographics and Clinical Characteristics

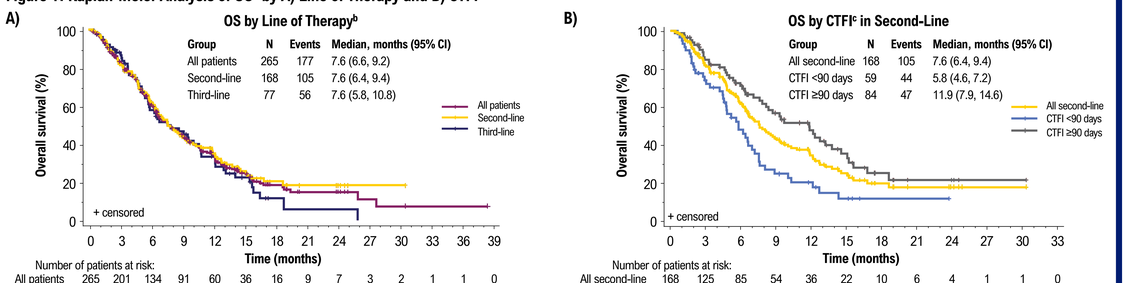
	All Patients N = 265
Age, median, years (range)	67.0 (29–89)
<65 years, n (%)	100 (38)
≥65 years, n (%)	165 (62)
Sex, n (%)	
Female	136 (51)
Male	129 (49)
Race, n (%)[a]	
American Indian/Alaska Native	2 (1)
Asian	7 (3)
Black or African American	23 (9)
White	223 (84)
Multiple	1 (0.4)
Ethnicity, n (%)[b]	
Hispanic or Latino	7 (3)
Not Hispanic or Latino	240 (91)
SCLC stage at initial diagnosis, n (%)	
Extensive	191 (72)
Limited	70 (26)
Missing	4 (2)

	All Patients N = 265
ECOG PS, n (%)	
0	45 (17)
1	133 (50)
2	44 (17)
3	7 (3)
Missing	36 (14)
CTFI, n (%)	
<30 days	52 (20)
30 to <90 days	35 (13)
90 to <180 days	64 (24)
≥180 days	73 (28)
Not calculated[c]	41 (15)
CNS metastases, n (%)	66 (25)
Liver metastases, n (%)	84 (32)
Line of therapy for lurbinectedin, n (%)[d]	
2L	168 (63)
3L	77 (29)

[a]Patients may report more than 1 race category; 9 patients declined to state their race. [b]Eighteen patients declined to state their ethnicity. [c]Did not have a reported progression date on first-line therapy. [d]Patients who received lurbinectedin as fourth-line or later therapy, or in combination with other anticancer therapies, are not reported due to the small number of patients.
2L, second-line; 3L, third-line; CNS, central nervous system; CTFI, chemotherapy-free interval; ECOG PS, Eastern Cooperative Oncology Group performance status; SCLC, small cell lung cancer.

- As of 4 February 2025, 265 patients received at least 1 cycle of lurbinectedin treatment and were followed up to 24 months
- Median (range) number of lurbinectedin cycles administered was 4 (1–33) with a median (range) duration of treatment of 91 (21–756) days in the overall population
  - Median number of lurbinectedin cycles administered and duration of treatment were similar between patients in the 2L and 3L settings and within the subgroups of interest
- At data cutoff, 250 (94%) patients discontinued treatment, 14 (5%) were ongoing on treatment, and 1 completed treatment
- Reasons for treatment discontinuation (per the discontinuation electronic data capture form) were disease progression (169 [68%]), death (25 [10%]), adverse events (AEs; 13 [5%]), physician decision (10 [4%]), withdrawal of consent (6 [2%]), lost to follow-up (3 [1%]), and other (24 [10%])

Figure 1. Kaplan-Meier Analysis of OS[a] by A) Line of Therapy and B) CTFI



[a]Some patients had OS follow-up >24 months and were noted as protocol deviations. [b]Additional patients received lurbinectedin as a fourth-line or later therapy or in combination with other anticancer therapies. [c]CTFI could not be calculated for patients who did not have a reported progression date on first-line therapy.
CI, confidence interval; CTFI, chemotherapy-free interval; OS, overall survival.

Table 5. OS by Line of Therapy and Subgroup

	All Patients N = 265[b]			CTFI <90 Days n = 87[b]		CTFI ≥90 Days n = 137[b]		Age <65 Years n = 100		Age ≥65 Years n = 165		No CNS Mets n = 199		CNS Mets n = 66	
	All N = 265	2L n = 168	3L n = 77	2L n = 59	3L n = 21	2L n = 84	3L n = 41	2L n = 60	3L n = 30	2L n = 108	3L n = 47	2L n = 124	3L n = 60	2L n = 44	3L n = 17
OS, median, months (95% CI)	7.6 (6.6, 9.2)	7.6 (6.4, 9.4)	7.6 (5.8, 10.8)	5.8 (4.6, 7.2)	5.5 (3.8, 6.8)	11.9 (7.9, 14.6)	8.7 (5.4, 12.2)	7.9 (7.0, 11.9)	9.6 (5.8, 13.2)	6.7 (5.8, 9.7)	6.6 (4.9, 10.8)	8.6 (6.4, 11.9)	8.7 (5.9, 12.2)	7.6 (5.6, 8.7)	5.5 (2.1, 10.6)

[a]Additional patients received lurbinectedin as a fourth-line or later therapy or in combination with other anticancer therapies. [b]CTFI could not be calculated for patients who did not have a reported progression date on first-line therapy.
2L, second-line; 3L, third-line; CNS Mets, central nervous system metastases; CTFI, chemotherapy-free interval; OS, overall survival.

- Longer median OS was observed with lurbinectedin treatment in patients with CTFI ≥90 days (vs <90 days), those younger than 65 years (vs ≥65 years), and those without CNS metastasis (vs with CNS metastases)

Table 3. Tumour Response and Progression-Free Survival in All Patients and by Subgroup

Tumour Responses Assessed per RECIST v1.1 in Patients With Measurable Disease at Baseline									
	All Patients N = 192[a]	2L Lurbinectedin n = 123	3L Lurbinectedin n = 57	CTFI <90 Days n = 64[b]	CTFI ≥90 Days n = 97[b]	Age <65 Years n = 71	Age ≥65 Years n = 121	No CNS Mets n = 150	CNS Mets n = 42
ORR, n (%) [95% CI]	51 (27) [20, 33]	36 (29) [21, 38]	13 (23) [13, 36]	14 (22) [13, 34]	28 (29) [20, 39]	19 (27) [17, 39]	32 (26) [19, 35]	44 (29) [22, 37]	7 (17) [7, 31]
BOR, n (%)									
CR	8 (4)	5 (4)	1 (2)	2 (3)	5 (5)	2 (3)	6 (5)	7 (5)	1 (2)
PR	43 (22)	31 (25)	12 (21)	12 (19)	23 (24)	17 (24)	26 (21)	37 (25)	6 (14)
SD	36 (19)	21 (17)	14 (25)	12 (19)	18 (19)	15 (21)	21 (17)	29 (19)	7 (17)
PD	72 (38)	46 (37)	20 (35)	21 (33)	37 (38)	28 (39)	44 (36)	52 (35)	20 (48)
PFS, median, months (95% CI)	3.3 (2.6, 4.1)	3.3 (2.4, 4.1)	3.8 (2.5, 4.9)	3.1 (2.1, 4.2)	3.1 (2.5, 4.2)	4.1 (2.8, 4.5)	2.9 (2.3, 4.0)	3.8 (2.7, 4.9)	2.5 (2.0, 3.5)
DoR, median, months (95% CI)	4.0 (3.0, 4.9)	3.7 (2.7, 4.8)	4.7 (2.7, 6.3)	3.7 (2.3, 4.8)	3.5 (2.6, 6.9)	4.7 (2.6, 6.4)	3.7 (2.7, 6.2)	4.4 (3.5, 6.3)	2.7 (0.7, 4.9)
DCR,[c] n (%) [95% CI]	87 (45) [38, 53]	57 (46) [37, 56]	27 (47) [34, 61]	26 (41) [29, 54]	46 (47) [37, 58]	34 (48) [26, 60]	53 (44) [35, 53]	73 (49) [40, 57]	14 (33) [20, 50]

[a]All patients with measurable disease at baseline, including those who received lurbinectedin as a fourth-line or later therapy or in combination with other anticancer therapies. [b]CTFI could not be calculated for patients who did not have a reported progression date on first-line therapy. [c]Disease control was defined as a BOR of CR, PR, or SD.
2L, second-line; 3L, third-line; BOR, best overall response; CI, confidence interval; CNS Mets, central nervous system metastases; CR, complete response; CTFI, chemotherapy-free interval; DCR, disease control rate; DoR, duration of response; ORR, overall response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumours version 1.1; SD, stable disease.

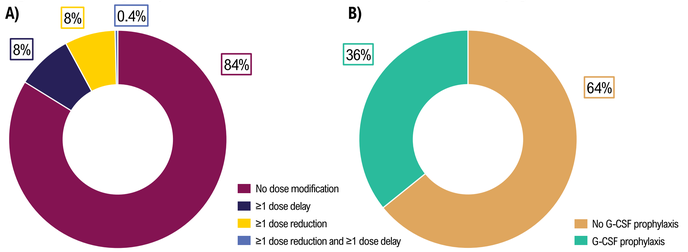
Table 4. Tumour Response and Progression-Free Survival by Lurbinectedin Line of Therapy in Patient Subgroups

Tumour Responses Assessed per RECIST v1.1 in Patients With Measurable Disease at Baseline											
	CTFI <90 Days		CTFI ≥90 Days		Age <65 Years		Age ≥65 Years		No CNS Mets		CNS Mets	
	2L n = 42	3L n = 18	2L n = 60	3L n = 29	2L n = 43	3L n = 23	2L n = 80	3L n = 34	2L n = 93	3L n = 46	2L n = 30	3L n = 11
ORR, n (%) [95% CI]	10 (24) [12, 39]	3 (17) [4, 41]	22 (37) [25, 50]	5 (17) [6, 36]	12 (28) [15, 44]	5 (22) [7, 44]	24 (30) [20, 41]	8 (24) [11, 41]	30 (32) [23, 43]	12 (26) [14, 41]	6 (20) [8, 39]	1 (9) [0, 41]
PFS, median, months (95% CI)	3.1 (2.0, 4.2)	3.8 (1.4, 6.3)	3.8 (2.3, 4.3)	2.9 (2.4, 4.7)	3.8 (2.1, 4.2)	4.7 (2.5, 5.3)	3.1 (2.1, 4.3)	3.5 (2.4, 4.9)	4.0 (2.4, 4.9)	4.5 (2.6, 5.3)	2.7 (1.6, 3.5)	2.1 (0.6, 4.4)
DoR, median, months (95% CI)	3.6 (1.5, 4.8)	4.7 (1.6, 6.3)	3.2 (2.3, 8.5)	3.5 (2.6, 6.2)	3.4 (1.5, 4.8)	4.9 (3.2, 6.4)	3.7 (2.7, 6.9)	3.5 (1.6, 6.2)	4.2 (2.7, 6.9)	3.5 (2.6, 6.3)	2.7 (0.7, 4.2)	4.9 (NE, NE)
DCR,[a] n (%) [95% CI]	18 (43) [28, 59]	7 (39) [17, 64]	32 (53) [40, 66]	12 (41) [24, 61]	20 (47) [31, 62]	11 (48) [27, 69]	37 (46) [35, 58]	16 (47) [30, 65]	46 (49) [39, 60]	24 (52) [37, 67]	11 (37) [20, 56]	3 (27) [6, 61]

[a]Disease control was defined as a best overall response of complete response, partial response, or stable disease.
2L, second-line; 3L, third-line; CI, confidence interval; CNS Mets, central nervous system metastases; CTFI, chemotherapy-free interval; DCR, disease control rate; DoR, duration of response; NE, not evaluable; ORR, overall response rate; PFS, progression-free survival; RECIST v1.1, Response Evaluation Criteria in Solid Tumours version 1.1.

- Numerically higher ORR was observed in patients treated with lurbinectedin in the 2L (vs 3L), those with CTFI ≥90 days (vs CTFI <90 days), and those without CNS metastasis (vs with CNS metastasis)
- Numerically longer median PFS was observed in patients younger than 65 years old and those without CNS metastasis

Figure 2. Summary of A) Lurbinectedin Dose Modifications and B) G-CSF Prophylaxis Use



G-CSF, granulocyte colony-stimulating factor.

- Dose modifications due to any reason occurred in 43 (16%) patients
  - Dose reductions (n = 21) were primarily caused by AEs (13 [62%])
  - Dose delays (n = 23) were caused by treatment delay >3 weeks from treatment due date (4 [2%]), intercurrent illness (2 [1%]), patient decision (2 [1%]), and other (15 [6%])
- Approximately one-third of patients were administered G-CSF prophylaxis

Table 6. Summary of Safety Outcomes in All Patients

n (%)	All Patients N = 265
Any AE	159 (60)
AE leading to discontinuation	18 (7)
AE leading to dose reduction	13 (5)
Any SAE	98 (37)
Treatment-related SAE	28 (11)
Any TRAE	86 (32)
TRAEs occurring in >5%, any grade	
Anaemia	21 (8)
Neutropenia	20 (8)
Thrombocytopenia	15 (6)
Nausea	15 (6)
Any AESI[a]	72 (27)
Any serious AESI	19 (7)
Injection-site reaction	5 (2)
Anaemia	4 (2)
Neutropenia	4 (2)
Neutropenic infection	4 (2)
Hepatic enzyme increase	2 (1)
Thrombocytopenia	2 (1)
Capillary leak syndrome	1 (0.4)
CPK elevations/rhabdomyolysis	1 (0.4)

[a]AESI includes grade 3/4 myelosuppression (including neutropenia, anaemia, and thrombocytopenia); acute infection (in the setting of grade ≥3 neutropenia); elevated liver enzymes; injection-site reaction; capillary leak syndrome; CPK elevations/rhabdomyolysis; and acute myeloid leukaemia/myelodysplasia.
AE, adverse event; AESI, AE of special interest; CPK, creatine phosphokinase; SAE, serious AE; TRAE, treatment-related AE.

- Thirty (11%) deaths occurred within 30 days of the last treatment administration

Conclusions

- Jazz EMERGE 402 enrolled a broader population of patients with SCLC than the phase 2 basket trial,[4] including those with poor prognostic factors, such as a CTFI <90 days, age ≥65 years, and CNS involvement; the study also included patients receiving lurbinectedin in the 3L setting
- Lurbinectedin demonstrated clinically meaningful effectiveness across subgroups, including as a 3L treatment and in older patients (≥65 years), those with platinum-resistant disease (CTFI <90 days), and those with CNS metastases; this contrasts with the poor outcomes observed with topotecan in these subgroups[6]
- Lurbinectedin was generally well tolerated in clinical practice, with no new safety signals and low rates of dose reductions and treatment discontinuations due to AEs
  - Serious haematological abnormalities were reported at lower rates than in the pivotal trial of lurbinectedin and in a real-world study of topotecan[4,6]
  - G-CSF prophylaxis use likely contributed to the low rates of neutropenia reported

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